

In the Specification:

On pages 2 and 3, please amend the paragraph beginning at line 37 of page 2 as follows:

AI  
In one embodiment, the invention features an isolated nucleic acid molecule that includes the nucleotide sequence set forth in SEQ ID NO:1 or SEQ ID NO:3. In another embodiment, the invention features an isolated nucleic acid molecule that encodes a polypeptide including the amino acid sequence set forth in SEQ ID NO:2. In another embodiment, the invention features an isolated nucleic acid molecule that includes the nucleotide sequence contained in the plasmid deposited with ATCC® as Accession Number [[\_\_\_\_]] PTA-3439.

On pages 10 and 11, please amend the paragraph beginning at line 32 of page 10 as follows:

AI  
For example, the family of DHDR-7 polypeptides disclosed herein comprise at least one "acyl-Co-A dehydrogenase domain." As used herein, the term "acyl-Co-A dehydrogenase domain" includes a protein domain having an amino acid sequence of about 250-450 amino acid residues, having a bit score of at least 100 when compared against an acyl-CoA dehydrogenase domain Hidden Marker Model (HMM), and which serves to catalyze the dehydrogenation of acyl-CoA esters. Preferably, an acyl-Co-A dehydrogenase domain includes at least about 353 amino acid residues and has a bit score of 399.8. To identify the presence of an acyl-Co-A dehydrogenase domain in a DHDR-7 protein, and make the determination that a protein of interest has a particular profile, the amino acid sequence of the protein may be searched against a database of known protein domains (*e.g.*, the HMM database). In one embodiment, an acyl-Co-A dehydrogenase domain, as defined herein, may comprise an acyl-Co-A dehydrogenase middle domain, an acyl-Co-A dehydrogenase C-terminal domain, and/or an acyl-Co-A dehydrogenase N-terminal domain. A search was performed against the HMM database resulting in the identification of a potential acyl-CoA dehydrogenase C-terminal domain in the amino acid sequence of human DHDR-7 at about residues 179-286 of SEQ ID NO:2, a potential acyl-CoA dehydrogenase middle domain in the amino acid sequence of human DHDR-7 at about residues 85-177 of SEQ ID NO:2, and a potential acyl-CoA dehydrogenase N-terminal domain in the amino acid sequence of human DHDR-7 at about residues 290-441 of SEQ ID NO:2. The acyl-CoA dehydrogenase C-terminal domain (HMM) has been assigned the PFAM Accession PF00441, the acyl-CoA dehydrogenase middle domain (HMM) has been assigned the PFAM Accession PF02770, and the acyl-CoA dehydrogenase N-terminal domain (HMM) has been assigned the PFAM Accession PF02771 (<http://genome.wustl.edu/Pfam/html>). The results of the search are set forth in Figure 2.

On page 12, please amend the paragraph beginning at line 4 as follows:

A3  
In a preferred embodiment, a DHDR-7 polypeptide includes at least one acyl-Co-A dehydrogenase domain and has an amino acid sequence at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more homologous or identical to the amino acid sequence of SEQ ID NO:2, or the amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]]PTA-3439. In yet another preferred embodiment, a DHDR-7 polypeptide includes at least one or more acyl-Co-A dehydrogenase domains, and is encoded by a nucleic acid molecule having a nucleotide sequence which hybridizes under stringent hybridization conditions to a complement of a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or SEQ ID NO:3. In another preferred embodiment, a DHDR-7 polypeptide includes at least one or more acyl-Co-A dehydrogenase domains, and has a DHDR-7 activity.

On pages 12 and 13, please amend the paragraph beginning at line 35 of page 12 as follows:

A4  
The nucleotide sequence of the isolated human DHDR-7 cDNA and the predicted amino acid sequence of the human DHDR-7 polypeptide are shown in Figure 1 and in SEQ ID NOs:1 and 2, respectively. A plasmid containing the nucleotide sequence encoding human DHDR-7 was deposited with the American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, VA 20110-2209, on [[\_\_\_\_]] June 7, 2001 and assigned Accession Number [[\_\_\_\_]] PTA-3439. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an admission that a deposit is required under 35 U.S.C. §112.

On pages 13 and 14, please amend the paragraph beginning at line 36 of page 13 as follows:

A5  
A nucleic acid molecule of the present invention, *e.g.*, a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, or a portion thereof, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, as a hybridization probe, DHDR-7 nucleic acid molecules can be isolated using standard hybridization and cloning techniques (*e.g.*, as described in Sambrook, J.,

Fritsh, E. F., and Maniatis, T. *Molecular Cloning: A Laboratory Manual*. 2nd, ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

On page 14, please amend the paragraph beginning at line 9 as follows:

A 6  
Moreover, a nucleic acid molecule encompassing all or a portion of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439 can be isolated by the polymerase chain reaction (PCR) using synthetic oligonucleotide primers designed based upon the sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439.

On pages 14 and 15, please amend the paragraph beginning at line 36 of page 14 as follows:

A 7  
In still another embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, or a portion of any of these nucleotide sequences. A nucleic acid molecule which is complementary to the nucleotide sequence shown in SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, is one which is sufficiently complementary to the nucleotide sequence shown in SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, such that it can hybridize to the nucleotide sequence shown in SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, thereby forming a stable duplex.

On page 15, please amend the paragraph beginning at line 10 as follows:

A 8  
In still another preferred embodiment, an isolated nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or more identical to the nucleotide sequence shown in SEQ ID NO:1 or 3 (e.g., to the entire length of the nucleotide sequence), or to the nucleotide sequence (e.g., the entire length of the nucleotide sequence) of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, or a portion of any of these nucleotide sequences. In one embodiment, a nucleic acid molecule of the present invention comprises a nucleotide sequence which is at least (or no greater than) 50-100, 100-250, 250-500,

500-750, 750-1000, 1000-1250, 1250-1500, 1500-1750, 1750-2000, 2000-2250, 2250-2500 or more nucleotides in length and hybridizes under stringent hybridization conditions to a complement of a nucleic acid molecule of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439.

On pages 15 and 16, please amend the paragraph beginning at line 24 of page 15 as follows:

A<sup>9</sup> Moreover, the nucleic acid molecule of the invention can comprise only a portion of the nucleic acid sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, for example, a fragment which can be used as a probe or primer or a fragment encoding a portion of a DHDR-7 polypeptide, *e.g.*, a biologically active portion of a DHDR-7 polypeptide. The nucleotide sequence determined from the cloning of the DHDR-7 gene allows for the generation of probes and primers designed for use in identifying and/or cloning other DHDR-7 family members, as well as DHDR-7 homologues from other species. The probe/primer typically comprises substantially purified oligonucleotide. The probe/primer (*e.g.*, oligonucleotide) typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12 or 15, preferably about 20 or 25, more preferably about 30, 35, 40, 45, 50, 55, 60, 65, 75, 80, 85, 90, 95, or 100 or more consecutive nucleotides of a sense sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, of an anti-sense sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, or of a naturally occurring allelic variant or mutant of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439.

On page 16, please amend the paragraph beginning at line 20 as follows:

A<sup>10</sup> A nucleic acid fragment encoding a "biologically active portion of a DHDR-7 polypeptide" can be prepared by isolating a portion of the nucleotide sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, which encodes a polypeptide having a DHDR-7 biological activity (the biological activities of the DHDR-7 polypeptides are described herein), expressing the encoded portion of the DHDR-7 polypeptide (*e.g.*, by recombinant expression *in vitro*) and assessing the activity of the encoded portion of the DHDR-7 polypeptide. In an exemplary embodiment, the nucleic acid molecule is at least 50-100, 100-250, 250-500, 500-750,

750-1000, 1000-1250, 1250-1500, 1500-1750, 1750-2000, 2000-2250, 2250-2500 or more nucleotides in length and encodes a polypeptide having a DHDR-7 activity (as described herein).

On pages 16 and 17, please amend the paragraph beginning at line 32 of page 16 as follows:

A<sup>11</sup>  
The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence shown in SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439. Such differences can be due to the degeneracy of the genetic code, thus resulting in a nucleic acid which encodes the same DHDR-7 polypeptides as those encoded by the nucleotide sequence shown in SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439. In another embodiment, an isolated nucleic acid molecule of the invention has a nucleotide sequence encoding a polypeptide having an amino acid sequence which differs by at least 1, but no greater than 5, 10, 20, 50, 100, or 200 amino acid residues from the amino acid sequence shown in SEQ ID NO:2, or the amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number [[\_\_\_\_]] PTA-3439. In yet another embodiment, the nucleic acid molecule encodes the amino acid sequence of human DHDR-7. If an alignment is needed for this comparison, the sequences should be aligned for maximum homology.

On page 17, please amend the paragraph beginning at line 22 as follows:

A<sup>12</sup>  
Accordingly, in one embodiment, the invention features isolated nucleic acid molecules which encode a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, wherein the nucleic acid molecule hybridizes to a complement of a nucleic acid molecule comprising SEQ ID NO:1 or SEQ ID NO:3, for example, under stringent hybridization conditions.

On page 18, please amend the paragraph beginning at line 10 as follows:

A<sup>13</sup>  
Moreover, nucleic acid molecules encoding other DHDR-7 family members and, thus, which have a nucleotide sequence which differs from the DHDR-7 sequences of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439 are intended to be within the scope of the invention. For example, another DHDR-7 cDNA can be identified based on the nucleotide sequence of human DHDR-7. Moreover, nucleic acid molecules encoding DHDR-7 polypeptides from

different species, and which, thus, have a nucleotide sequence which differs from the DHDR-7 sequences of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439 are intended to be within the scope of the invention. For example, a hamster DHDR-7 cDNA can be identified based on the nucleotide sequence of a human DHDR-7.

On page 18, please amend the paragraph beginning at line 28 as follows:

A<sup>14</sup>  
Orthologues, homologues and allelic variants can be identified using methods known in the art (*e.g.*, by hybridization to an isolated nucleic acid molecule of the present invention, for example, under stringent hybridization conditions). In one embodiment, an isolated nucleic acid molecule of the invention is at least 15, 20, 25, 30 or more nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439. In other embodiments, the nucleic acid is at least 50-100, 100-250, 250-500, 500-750, 750-1000, 1000-1250, 1250-1500, 1500-1750, 1750-2000, 2000-2250, 2250-2500 or more nucleotides in length.

On page 20, please amend the paragraph beginning at line 8 as follows:

A<sup>15</sup>  
In addition to naturally-occurring allelic variants of the DHDR-7 sequences that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequences of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, thereby leading to changes in the amino acid sequence of the encoded DHDR-7 polypeptides, without altering the functional ability of the DHDR-7 polypeptides. For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in the sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439. A "non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of DHDR-7 (*e.g.*, the sequence of SEQ ID NO:2) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino acid residues that are conserved among the DHDR-7 polypeptides of the present invention, *e.g.*, those present in an acyl-CoA dehydrogenase domain, are predicted to be particularly unamenable to alteration. Furthermore, additional amino acid residues that are conserved between the DHDR-7 polypeptides of the present invention and other members of the DHDR-7 family are not likely to be amenable to alteration.

On pages 20 and 21, please amend the paragraph beginning at line 34 of page 20 as follows:

A<sup>16</sup>  
An isolated nucleic acid molecule encoding a DHDR-7 polypeptide identical to the polypeptide of SEQ ID NO:2, can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, such that one or more amino acid substitutions, additions or deletions are introduced into the encoded polypeptide. Mutations can be introduced into SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439 by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (*e.g.*, lysine, arginine, histidine), acidic side chains (*e.g.*, aspartic acid, glutamic acid), uncharged polar side chains (*e.g.*, glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (*e.g.*, alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (*e.g.*, threonine, valine, isoleucine) and aromatic side chains (*e.g.*, tyrosine, phenylalanine, tryptophan, histidine). Thus, a predicted nonessential amino acid residue in a DHDR-7 polypeptide is preferably replaced with another amino acid residue from the same side chain family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a DHDR-7 coding sequence, such as by saturation mutagenesis, and the resultant mutants can be screened for DHDR-7 biological activity to identify mutants that retain activity. Following mutagenesis of SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, the encoded polypeptide can be expressed recombinantly and the activity of the polypeptide can be determined.

On pages 23 and 24, please amend the paragraph beginning at line 27 of page 23 as follows:

A<sup>17</sup>  
In still another embodiment, an antisense nucleic acid of the invention is a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (*e.g.*, hammerhead ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave DHDR-7 mRNA transcripts to

thereby inhibit translation of DHDR-7 mRNA. A ribozyme having specificity for a DHDR-7-encoding nucleic acid can be designed based upon the nucleotide sequence of a DHDR-7 cDNA disclosed herein (*i.e.*, SEQ ID NO:1 or 3, or the nucleotide sequence of the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in a DHDR-7-encoding mRNA. See, *e.g.*, Cech *et al.* U.S. Patent No. 4,987,071; and Cech *et al.* U.S. Patent No. 5,116,742. Alternatively, DHDR-7 mRNA can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, *e.g.*, Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

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On page 27, please amend the paragraph beginning at line 18 as follows:

A 18  
Another aspect of the invention features fragments of the polypeptide having the amino acid sequence of SEQ ID NO:2, for example, for use as immunogens. In one embodiment, a fragment comprises at least 5 amino acids (*e.g.*, contiguous or consecutive amino acids) of the amino acid sequence of SEQ ID NO:2, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number [[\_\_\_\_]] PTA-3439. In another embodiment, a fragment comprises at least 10, 15, 20, 25, 30, 35, 40, 45, 50 or more amino acids (*e.g.*, contiguous or consecutive amino acids) of the amino acid sequence of SEQ ID NO:2, or an amino acid sequence encoded by the DNA insert of the plasmid deposited with the ATCC as Accession Number [[\_\_\_\_]] PTA-3439.

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On page 28, please amend the paragraph beginning at line 24 as follows:

A 19  
The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid sequences is determined using the Needleman and Wunsch (*J. Mol. Biol.* (48):444-453 (1970)) algorithm which has been incorporated into the GAP program in the GCG software package (~~available at <http://www.gcg.com>~~), using either a Blosum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. In yet another preferred embodiment, the percent identity between two nucleotide sequences is determined using the GAP program in the GCG software package (~~available at <http://www.gcg.com>~~), using a NWSgapdna.CMP matrix and a gap weight of 40, 50, 60, 70, or 80 and a length weight of 1, 2, 3, 4, 5, or 6. A preferred, non-limiting example of parameters to be used in conjunction with the GAP program include a Blosum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.



On page 29, please amend the paragraph beginning at line 4 as follows:

A20  
The nucleic acid and polypeptide sequences of the present invention can further be used as a "query sequence" to perform a search against public databases to, for example, identify other family members or related sequences. Such searches can be performed using the NBLAST and XBLAST programs (version 2.0) of Altschul, *et al.* (1990) *J. Mol. Biol.* 215:403-10. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to DHDR-7 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST program, score = 100, wordlength = 3, and a Blosum62 matrix to obtain amino acid sequences homologous to DHDR-7 polypeptide molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul *et al.*, (1997) *Nucleic Acids Res.* 25(17):3389-3402. When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (*e.g.*, XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>.

On pages 41 and 42, please amend the paragraph beginning at line 17 of page 41 as follows:

A21  
A transgenic animal of the invention can be created by introducing a DHDR-7-encoding nucleic acid into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The DHDR-7 cDNA sequence of SEQ ID NO:1 can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of a human DHDR-7 gene, such as a mouse or rat DHDR-7 gene, can be used as a transgene. Alternatively, a DHDR-7 gene homologue, such as another DHDR-7 family member, can be isolated based on hybridization to the DHDR-7 cDNA sequences of SEQ ID NO:1 or 3, or the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439 (described further in subsection I above) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to a DHDR-7 transgene to direct expression of a DHDR-7 polypeptide to particular cells. Methods for generating transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, both by Leder *et al.*, U.S. Patent No. 4,873,191 by Wagner *et al.* and in Hogan, B., *Manipulating the Mouse Embryo*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder

animal can be identified based upon the presence of a DHDR-7 transgene in its genome and/or expression of DHDR-7 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding a DHDR-7 polypeptide can further be bred to other transgenic animals carrying other transgenes.

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On page 66, please amend the paragraph beginning at line 3 as follows:

A<sup>22</sup> An exemplary method for detecting the presence or absence of DHDR-7 polypeptide or nucleic acid in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting DHDR-7 polypeptide or nucleic acid (*e.g.*, mRNA, or genomic DNA) that encodes DHDR-7 polypeptide such that the presence of DHDR-7 polypeptide or nucleic acid is detected in the biological sample. In another aspect, the present invention provides a method for detecting the presence of DHDR-7 activity in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of DHDR-7 activity such that the presence of DHDR-7 activity is detected in the biological sample. A preferred agent for detecting DHDR-7 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to DHDR-7 mRNA or genomic DNA. The nucleic acid probe can be, for example, the DHDR-7 nucleic acid set forth in SEQ ID NO:1 or 3, or the DNA insert of the plasmid deposited with ATCC as Accession Number [[\_\_\_\_]] PTA-3439, or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent conditions to DHDR-7 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

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On pages 83 and 84, please amend the paragraph beginning at line 37 of page 83 as follows:

A<sup>23</sup> The invention is based, at least in part, on the discovery of a human gene encoding a novel polypeptide, referred to herein as human DHDR-7. The entire sequence of the human clone Fbh62112 was determined and found to contain an open reading frame termed human "DHDR-7." The nucleotide sequence of the human DHDR-7 gene is set forth in Figure 1 and in the Sequence Listing as SEQ ID NO:1. The amino acid sequence of the human DHDR-7 expression product is set forth in Figure 1 and in the Sequence Listing as SEQ ID NO: 2. The DHDR-7 polypeptide comprises about 621 amino acids. The coding region (open reading frame) of SEQ ID NO:1 is set forth as SEQ ID NO:3. Clone Fbh62112FL, comprising the coding region of human DHDR-7, was deposited with the American Type Culture Collection (ATCC®),

10801 University Boulevard, Manassas, VA 20110-2209, on [[\_\_\_\_]] June 7, 2001, and assigned Accession No. [[\_\_\_\_]] PTA-3439.

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On page 84, please amend the paragraph beginning at line 22 as follows:

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A 24  
The amino acid sequence of human DHDR-7 was analyzed using the program PSORT (<http://www.psорт.nibb.ac.jp>) to predict the localization of the protein within the cell. This program assesses the presence of different targeting and localization amino acid sequences within the query sequence. The results of this analysis show that human DHDR-7 may be localized to the mitochondria, the cytoplasm, and the nucleus.

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